

Continuation of Application No. 09/761,903
Docket No. X-11232B

86. (New) The microcrystal of Claim 85, wherein the complexing compound is protamine which is present at about 0.15 mg to about 0.5 mg per 3.5 mg of B29-Nε-tetradecanoyl-des(B30)-human insulin.

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87. (New) The microcrystal of Claim 86, wherein the divalent metal cation is zinc, which is present at about 0.3 mole to about 0.7 mole per mole of B29-Nε-tetradecanoyl-des(B30)-human insulin.

88. (New) The microcrystal of Claim 87, wherein the hexamer-stabilizing compound is a phenolic preservative selected from the group consisting of phenol, m-cresol, o-cresol, p-cresol, chlorocresol, methylparaben, and mixtures thereof and is present in sufficient proportions with respect to the B29-Nε-tetradecanoyl-des(B30)-human insulin to facilitate formation of the R6 hexamer conformation.

89. (New) The microcrystal of Claim 85, wherein the microcrystal has rod-like morphology.

90. (New) The microcrystal of Claim 85, wherein the microcrystal has irregular morphology.

91. (New) A suspension formulation comprising an insoluble phase and a solution phase, wherein the insoluble phase is comprised of the microcrystal of Claim 85, and the solution phase is comprised of water.

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92. (New) A suspension formulation comprising an insoluble phase and a solution phase, wherein the insoluble phase is comprised of the microcrystal of Claim 86 and the solution phase is comprised of water.

93. (New) The suspension formulation of Claim 92, wherein the solution phase is further comprised of a phenolic preservative at a concentration of about 0.5 mg per mL to about 6 mg per mL of solution, a pharmaceutically acceptable buffer, and an isotonicity agent.

94. (New) The suspension formulation of Claim 93, wherein the solution phase is further comprised of insulin, an insulin analog, an acylated insulin, or an acylated insulin analog.

95. (New) The suspension formulation of Claim 94, wherein the solution phase is comprised of insulin.

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96. (New) The suspension formulation of Claim 96,
wherein the solution phase is comprised of an insulin analog.

97. (New) The suspension formulation of Claim 96,
wherein the insulin analog is a monomeric insulin analog.

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Cont. 98. (New) The suspension formulation of Claim 97,
wherein the insulin analog is LysB28,ProB29-human insulin
analog.

99. (New) The suspension formulation of Claim 91,
wherein the solution phase is further comprised of zinc and
protamine, wherein the ratio of zinc to B29-Nε-tetradecanoyl-
des(B30)-human insulin in the suspension formulation is from
about 5 to about 7 mole of zinc atoms per mole of B29-Nε-
tetradecanoyl-des(B30)-human insulin, and the ratio of
protamine to B29-Nε-tetradecanoyl-des(B30)-human insulin in
the suspension formulation is from about 0.25 mg to about 0.5
mg per mg of B29-Nε-tetradecanoyl-des(B30)-human insulin.

100. (New) A process for preparing the microcrystal of
Claim 85 comprising:

a) dissolving B29-Nε-tetradecanoyl-des(B30)-human
insulin, a hexamer-stabilizing compound, and a divalent metal

cation in an aqueous solvent having a pH that will permit the formation of hexamers of B29-Nε-tetradecanoyl-des(B30)-human insulin, and

- b) adding a complexing compound.

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101. (New) A process for preparing the microcrystal of Claim 85 comprising:

a) dissolving B29-Nε-tetradecanoyl-des(B30)-human insulin, a hexamer-stabilizing compound, and a divalent metal cation in an aqueous solvent having a pH that will not permit the formation of hexamers of B29-Nε-tetradecanoyl-des(B30)-human insulin, and

b) adjusting the pH to between about 6.8 and about 7.8; and

c) adding a complexing compound.

102. (New) A method of treating diabetes comprising administering the formulation of Claim 91 to a patient in need thereof in a quantity sufficient to regulate blood glucose levels in the patient.

103. (New) An amorphous precipitate comprising:

- a) B29-Nε-tetradecanoyl-des(B30)-human insulin;
b) a complexing compound;

- c) a hexamer-stabilizing compound; and
- d) a divalent metal cation.

104. (New) The amorphous precipitate of Claim 103,
wherein the complexing compound is protamine which is present
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at about 0.15 mg to about 0.5 mg per 3.5 mg of B29-Nε-
tetradecanoyl-des(B30)-human insulin.
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105. (New) The amorphous precipitate of Claim 104,
wherein the divalent metal cation is zinc, which is present at
about 0.3 mole to about 0.7 mole per mole of B29-Nε-
tetradecanoyl-des(B30)-human insulin.

106. (New) The amorphous precipitate of Claim 105,
wherein the hexamer-stabilizing compound is a phenolic
preservative selected from the group consisting of phenol, m-
cresol, o-cresol, p-cresol, chlorocresol, methylparaben, and
mixtures thereof and is present in sufficient proportions with
respect to the B29-Nε-tetradecanoyl-des(B30)-human insulin to
facilitate formation of the R6 hexamer conformation.

107. (New) A suspension formulation comprising an
insoluble phase and a solution phase, wherein the insoluble
phase is comprised of the amorphous precipitate of Claim 103,
and the solution phase is comprised of water.

108. (New) A suspension formulation comprising an insoluble phase and a solution phase, wherein the insoluble phase is comprised of the amorphous precipitate of Claim 104 and the solution phase is comprised of water.

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109. (New) The suspension formulation of Claim 108, wherein the solution phase is further comprised of a phenolic preservative at a concentration of about 0.5 mg per mL to about 6 mg per mL of solution, a pharmaceutically acceptable buffer, and an isotonicity agent.

110. (New) The suspension formulation of Claim 109, wherein the solution phase is further comprised of insulin, an insulin analog, an acylated insulin, or an acylated insulin analog.

111. (New) The suspension formulation of Claim 111, wherein the solution phase is comprised of insulin.

112. (New) The suspension formulation of Claim 110, wherein the solution phase is comprised of an insulin analog.

113. (New) The suspension formulation of Claim 112, wherein the insulin analog is a monomeric insulin analog.

114. (New) The suspension formulation of Claim 113,
wherein the insulin analog is LysB28,ProB29-human insulin
analog.

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CONT

115. (New) The suspension formulation of Claim 107,
wherein the solution phase is further comprised of zinc and
protamine, wherein the ratio of zinc to B29-Nε-tetradecanoyl-
des(B30)-human insulin in the suspension formulation is from
about 5 to about 7 mole of zinc atoms per mole of B29-Nε-
tetradecanoyl-des(B30)-human insulin, and the ratio of
protamine to B29-Nε-tetradecanoyl-des(B30)-human insulin in
the suspension formulation is from about 0.25 mg to about 0.5
mg per mg of B29-Nε-tetradecanoyl-des(B30)-human insulin.

116. (New) A process for preparing the amorphous
precipitate of Claim 104 comprising:

- a) dissolving B29-Nε-tetradecanoyl-des(B30)-human
insulin, a hexamer-stabilizing compound, and a divalent metal
cation in an aqueous solvent having a pH that will permit the
formation of hexamers of B29-Nε-tetradecanoyl-des(B30)-human
insulin, and
- b) adding a complexing compound.

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117. (New) A process for preparing the amorphous precipitate of Claim 104 comprising:

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- a) dissolving B29-Nε-tetradecanoyl-des(B30)-human insulin, a hexamer-stabilizing compound, and a divalent metal cation in an aqueous solvent having a pH that will not permit the formation of hexamers of B29-Nε-tetradecanoyl-des(B30)-human insulin, and
 - b) adjusting the pH to between about 6.8 and about 7.8; and
 - c) adding a complexing compound.

118. (New) A method of treating diabetes comprising administering the formulation of Claim 107 to a patient in need thereof in a quantity sufficient to regulate blood glucose levels in the patient.--

Remarks

I. STATUS OF THE CLAIMS

Claims 1-84 have been canceled, and new claims 85-118 have been added. Claims 85-118 are pending in the present application.